PRVD2008-07

Proposed Re-evaluation Decision

Bromoxynil

(publié aussi en français)

22 January 2008

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6605C
Ottawa, Ontario
K1A 0K9

Internet: pmra_publications@hc-sc.gc.ca
www.pmra-arla.gc.ca
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra_infoserv@hc-sc.gc.ca

Canada

ISBN: 978-0-662-47706-8 (978-0-662-47707-5)
Catalogue number: H113-27/2008-7E (H113-27/2008-7E-PDF)

© Her Majesty the Queen in Right of Canada, represented by the Minister of Health Canada, 2008

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of the Minister of Public Works and Government Services Canada, Ottawa, Ontario K1A 0S5.

Table of Contents

Overview 1

What is the Proposed Re-evaluation Decision? 1
- What did Health Canada Consider when Making this Re-evaluation Decision? 1
- What is Bromoxynil? 2
- Health Considerations 2
- Maximum Residue Limits 3
- Environmental Considerations 3
- Measures to Minimize Risk 4
- What Additional Scientific Information is Being Requested? 4
- Next Steps 4

Science Evaluation 5

1.0 Introduction 5

2.0 The Technical Grade Active Ingredient, Its Properties and Uses 5
- 2.1 Identity of the Technical Grade Active Ingredient (TGAI) 5
- 2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient 6
- 2.3 Comparison of Use Patterns in Canada and the United States 7

3.0 Impact on Human Health and the Environment 7
- 3.1 Human Health 8
  - 3.1.1 Occupational Exposure and Risk Assessment 8
  - 3.1.2 Aggregate Exposure and Risk Assessment 12
  - 3.1.3 Cumulative Effects 16
- 3.2 Environment 17
  - 3.2.1 Environmental Risk Assessment 17
  - 3.2.2 Toxic Substances Management Policy Considerations 20

4.0 OECD Status of Bromoxonil 21

5.0 Proposed Regulatory Decision 22

6.0 Data Required as Condition of Continued Registration 23

List of Abbreviations 25

Appendix I Registered Bromoxynil Products as of 31 July 2007 27

Appendix II Summary of Toxicological Endpoints Selected by the USEPA for Bromoxynil Health Risk Assessment 31

Appendix III Label Amendments for Products Containing Bromoxynil 33

Appendix IV Inputs to Buffer Zone Models 37

Overview

What is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide bromoxynil, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is proposing continued registration of bromoxynil products for the sale and use in Canada.

An evaluation of available scientific information found that bromoxynil products do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of bromoxynil uses, new risk-reduction measures must be included on the labels of bromoxynil products. No additional data are being requested as a result of this evaluation.

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products, to ensure they meet modern standards established to protect human health and the environment.

This proposal affects all end-use products containing bromoxynil registered in Canada. Once the final re-evaluation decision is made, registrants will be instructed on how to address any new requirements.

This *Proposed Re-evaluation Decision* is a consultation document[1] that summarizes the science evaluation for bromoxynil and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of bromoxynil.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

What did Health Canada Consider when Making this Re-evaluation Decision?

Health Canada's Pest Management Regulatory Agency is re-evaluating active ingredients and their uses to determine their continuing acceptability in relation to human health and the environment and value. Bromoxynil is one of the active ingredients to be re-evaluated during the current re-evaluation cycle. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

---

[1] "Consultation statement" as required by subsection 28(2) - *Pest Control Products Act* 2002

Bromoxynil has been re-evaluated under Re-evaluation Program 1, which relies as much as possible on foreign reviews, typically, United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, there must be a suitable foreign review that meets the following conditions:

- It covers the main science areas, such as human health and the environment, that are necessary for Canadian regulatory decisions.
- It addresses the active ingredient and the main formulation types registered in Canada.
- It is relevant to registered Canadian uses.

Based on the outcome of foreign reviews, the PMRA will propose, under Program 1, a regulatory decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account Canadian use pattern and issues (e.g. the Federal Toxic Substances Management Policy (TSMP)). A review of the chemistry of Canadian products is also conducted.

The USEPA conducted a re-evaluation of bromoxynil and conclusions of this re-evaluation are published in a 1998 RED. On the basis of health and environmental risk assessments, the USEPA concluded that bromoxynil was eligible for reregistration with implementation of risk-reduction measures. Based on a comparison of American and Canadian use patterns, the USEPA assessments described in this RED document were considered to be an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation Section of this consultation document.

What is Bromoxynil?

Bromoxynil is a herbicide that is used for the control of annual weeds in industrial oil seed crops and several terrestrial food and feed crops. Bromoxynil is applied using a variety of ground equipment by farm workers and professional applicators.

Health Considerations

Can Approved Uses of Bromoxynil Affect Human Health?

Additional risk-reduction measures are required on bromoxynil labels. Bromoxynil is unlikely to affect your health when used according to revised label directions.

Exposure to bromoxynil may occur through diet (food and water) when working as a mixer/loader/applicator or entering treated sites. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that bromoxynil was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions were considered applicable to the Canadian situation and equivalent risk-reduction measures are required.

Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Bromoxynil is currently registered in Canada for use on wheat, oats, barley, bromoxynil-tolerant canola, corn, flax, rye, garlic, alfalfa, millet and sorghum, and grasses grown for seed. As noted, bromoxynil may be used on other crops in other countries that are imported into Canada. An MRL of 0.1 parts per million (ppm) bromoxynil and its metabolite has been established for eggs, meat and meat byproducts of cattle and poultry, milk and rapeseed (canola). Where no specific MRL has been established, a general MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be promulgated.

Environmental Considerations

What Happens When Bromoxynil is Introduced Into the Environment?

Additional risk-reduction measures are required on bromoxynil labels. Bromoxynil is unlikely to affect non-target organisms when used according to revised label directions.

Non-target organisms (e.g. birds, mammals, insects, aquatic organisms and terrestrial plants) may be exposed to bromoxynil in the environment. Environmental risk is assessed by the risk quotient method, in which a risk quotient (RQ) is calculated as the ratio of the estimated environmental concentration (EEC) to the relevant effects endpoint of concern. The resulting RQs are compared to corresponding levels of concern (LOCs). An RQ less than the LOC is considered a negligible risk to non-target organisms, whereas an RQ greater than the LOC indicates some degree of risk.

The USEPA concluded that the reregistration of bromoxynil was acceptable, provided risk-reduction measures to further protect the environment were implemented. These conclusions were considered applicable to the Canadian situation, and equivalent

risk-reduction measures are required. Furthermore, the PMRA will require aquatic and terrestrial buffer zones for the emulsifiable concentrate and emulsion formulations to protect aquatic organisms and terrestrial plants from spray drift.

Measures to Minimize Risk

Registered pesticide product labels contain specific directions for use, which include risk-reduction measures to protect human and environmental health. These directions are required by law to be followed. As a result of the re-evaluation of bromoxynil, further risk-reduction measures are proposed in addition to those already identified on existing bromoxynil product labels. These additional measures are designed to further protect human health and the environment and are summarized as follows:

Human Health

- to protect mixer/loader/applicators: additional protective equipment
- to protect workers re-entering treated sites: a restricted entry interval

Environment

- to reduce potential surface and groundwater contamination: additional advisory label statements
- to protect non-target sensitive aquatic and terrestrial plants: buffer zones for aquatic and terrestrial habitats

What Additional Scientific Information is Being Requested?

No data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*.

Next Steps

Before making a final re-evaluation decision on bromoxynil, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision document, which will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

Science Evaluation

1.0 Introduction

Bromoxynil is a nitrile herbicide that acts by inhibition of photosynthetic electron transport and also uncouples oxidative phosphorylation in mitochondria, thereby stopping energy production and negatively affecting plant respiration.

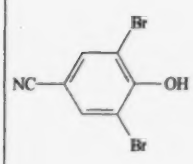
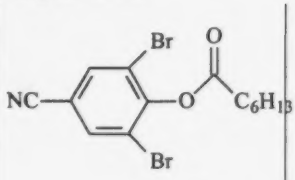
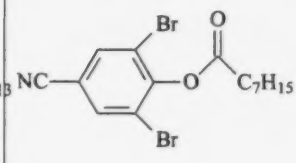
Following the re-evaluation announcement for bromoxynil, the registrant of the technical grade active ingredient in Canada indicated that it intended to provide continued support for certain uses currently registered in Canada.

The PMRA used recent assessments of bromoxynil from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for bromoxynil, dated September 1998, as well as other information on the regulatory status of bromoxynil in the United States, can be found on the USEPA's website at www.regulations.gov/fdmspublic/component/main.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient (TGAI)

	Bromoxynil Phenol	Bromoxynil Heptanoate	Bromoxynil Octanoate
Common Name	Bromoxynil	Bromoxynil Heptanoate	Bromoxynil Octanoate
1. International Union of Pure and Applied Chemistry (IUPAC) Chemical Name:	3,5-dibromo-4-hydroxybenzonitrile; 3,5-dibromo-4-hydroxyphenyl cyanide	2,6-dibromo-4-cyanophenyl heptanoate	2,6-dibromo-4-cyanophenyl octanoate
2. Chemical Abstracts Service (CAS) Chemical Name:	3,5-dibromo-4-hydroxybenzonitrile	2,6-dibromo-4-cyanophenyl heptanoate	2,6-dibromo-4-cyanophenyl octanoate
CAS Number	1689-84-5	56634-95-8	1689-99-2

	Bromoxynil Phenol	Bromoxynil Heptanoate	Bromoxynil Octanoate
Structural Formula			
Molecular Formula	$C_7H_3Br_2NO$	$C_{14}H_{15}Br_2NO_2$	$C_{15}H_{17}Br_2NO_2$
Molecular Weight	276.9	389.1	403.1
Registration Number and Purity of the TGAI:	19693 - 97.5% 19975 - 98.5% 21926 - 98.0%	19700 - 68.2%	21297 - 65.5% 19705 - 64.6% 19978 - 66.3% 27675 - 66.1%

Based on the manufacturing process, the product is not expected to contain impurities of human health or environmental concern as identified in Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4 or Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, Appendix II.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result		
	Bromoxynil Phenol	**Bromoxynil Heptanoate**	**Bromoxynil Octanoate**
Water solubility	130 mg/L (20°C)	~ 3 mg/L (25°C)	3 mg/L (25°C)
Vapour pressure	6.3×10^{-3} mPa (20°C)	~ 1.9×10^{-1} mPa	1.9×10^{-1} m Pa (25°C)
Dissociation constant (pK_a)	pKa = 3.86	No dissociation	No dissociation
n-Octanol–water partition coefficient (K_{ow})	Log K_{ow} = 2.8	Log K_{ow} =5.4	Log K_{ow} =5.4
UV/visible absorption spectrum	Not expected to absorb UV at λ>300 nm	Not expected to absorb UV at λ>300 nm	Not expected to absorb UV at λ>300 nm

2.3 Comparison of Use Patterns in Canada and the United States

Bromoxynil is a nitrile herbicide that is used for the control of annual weeds. There are three forms of bromoxynil registered in Canada; the ester of the N-heptanoic acid (bromoxynil heptanoate), the ester of the N-octanoate acid (bromoxynil octanoate) and bromoxynil phenol. Canadian end-use products may contain bromoxynil octanoate, bromoxynil heptanoate or a mixture of the two esters. The registered end-use products are formulated as emulsions or emulsifiable concentrates and may contain more than one active ingredient and be registered for a variety of tank mixes. Both bromoxynil octanoate and heptanoate are registered for postemergent commercial use in Canada on industrial oil seed crops and terrestrial food and feed crops. These include wheat, oats, barley, bromoxynil-tolerant canola, corn, flax, rye, garlic, alfalfa, millet and sorghum and grasses grown for seed. There is pre-emergence label use for minimum or zero till cultivation of wheat, barley and oats only. Methods of application are by groundboom and aerial, with a maximum application of 337 g a.i./ha. Application by groundboom equipment is typically once per year, the exceptions being established alfalfa, corn, barley, wheat and oats, which have a maximum of two annual applications. Aerial application is limited to wheat, oats and barley and, for the most part, once per year up to 281.3 g a.i./ha. Two end-use products (registration numbers 14878 and 18001) allow for a maximum of two aerial applications on barley and wheat only at 280 and 337 g a.i./ha, respectively.

A comparison of U.S. and Canadian use patterns was conducted. Bromoxynil is registered for commercial uses in both Canada and the U.S. Residential use is not registered for either country. The formulation types and forms (specifically, bromoxynil phenol, bromoxynil octanoate, bromoxynil heptanoate and ester mixtures) of Canadian products are encompassed by those eligible for reregistration in the U.S. Although a decision of eligibility for reregistration was not made by the USEPA for products containing the heptanoate ester only, a decision was made for products with both esters. However, there were sufficient data on the heptanoate ester in the RED, to make a re-evaluation decision for Canadian products formulated with bromoxynil heptanoate only. All Canadian products are thus encompassed by those eligible for reregistration in the U.S. All current Canadian uses, except for the use on bromoxynil-tolerant canola, are being supported by the registrants and were therefore considered in the re-evaluation of bromoxynil. Appendix I lists all bromoxynil products that are registered under the authority of the *Pest Control Products Act*.

Based on this comparison of use patterns, it was concluded that the USEPA RED for bromoxynil is an adequate basis for the re-evaluation of Canadian uses of bromoxynil.

3.0 Impact on Human Health and the Environment

The USEPA conducted a re-evaluation of bromoxynil and published its conclusions in a 1998 RED. In this document, the USEPA concluded that the end-use products formulated with bromoxynil met the safety standard under the U.S. *Food Quality Protection Act* (FQPA) amendments and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended labels of all end-use products containing bromoxynil.

Application methods and rates used in Canada are among those assessed in the RED. Canadian use sites are encompassed by the U.S. use pattern, except for the single product label use on canola (registrants have indicated intent to remove this use from Canadian labels). The U.S. use pattern is more extensive than in Canada, with uses registered on sod farms, cotton and ornamental trees and lawn/turf.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels where no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to bromoxynil may occur through consumption of food and water, working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, two key factors are considered: the levels where no health effects occur, and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

For purposes of assessing risk to human health, the USEPA concluded that both esters of the chemical are toxicologically equivalent on a molar basis. From animal metabolism studies involving both the heptanoate and octanoate ester, it was concluded that both esters are rapidly and nearly completely converted to bromoxynil phenol in vivo, and the pharmokinetic behaviour, metabolism, distribution and excretion of all three compounds are essentially identical in the animal body.

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures, with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but measures to mitigate (reduce) risk would be required. In the case where evidence of carcinogenicity is identified for the active, a cancer potency factor (Q_1*) is generated and used to estimate cancer risk. The product of the expected exposure and the cancer potency factor (Q_1*) estimates the lifetime cancer risk as a probability. A lifetime cancer risk in the range of 1 in 10^{-5} to 1 in 10^{-6} in worker populations is generally considered acceptable. The toxicological endpoints selected by the USEPA for assessment of risk from occupational exposure are summarized in Appendix II.

Workers can be exposed to bromoxynil through mixing, loading or applying the pesticide and when re-entering a treated site to conduct activities such as scouting and/or handling of treated crops.

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

Although a chronic (non-cancer) endpoint was identified for bromoxynil, based on its use pattern a chronic-term exposure/risk assessment was not conducted as chronic exposure is unlikely.

The following potential exposure scenarios assessed by the USEPA were relevant to the Canadian use patterns.

Private Handlers

- mixing/loading liquids for groundboom applications
- mixing/loading liquids for aerial applications
- groundboom applications
- mixing/loading/applying liquid formulations by groundboom
- aerial applications

Commercial Handlers

- mixing/loading liquids for groundboom applications
- mixing/loading liquids for aerial applications
- groundboom applications
- aerial applications

Determinations were made for the private handlers (i.e. farmers) who typically make one or two applications per year and for commercial handlers (i.e. custom applicators) making 10 or more applications per year. Surrogate data from PHED V1.1 were used to estimate dermal exposure for handlers, and inhalation was considered negligible. The cancer risk was determined using an oral toxicity endpoint and thus required a dermal absorption factor (10%). An MOE of 100 was considered appropriate for short- and intermediate-term exposure. No distinction was made between private and commercial handlers for calculation of short- and intermediate-term exposure risks. Risk determinations (short- and intermediate-term), which encompassed those scenarios above for the private grower, were made for all crops at the maximum rate of 0.565 kg a.i./ha.

The calculations of risk indicated that the MOEs for short- and intermediate-term exposures were greater than 100 (ranged from 140–2300) for all scenarios, either with baseline attire (long pants, long-sleeved shirt, shoes, socks) or in the case of mixers/loaders, when chemical-resistant gloves are worn.

Cancer risks were determined for private and commercial handlers for all potential exposure scenarios using specific rates (based on typical annual usage), acreage treated per day and treatments per year for each crop.

Results for scenarios listed above were as follows:

Groundboom

For groundboom, typical rates assessed were as follows:

- 0.224 kg a.i./ha wheat
- 0.344 kg a.i./ha barley, flax, sorghum, cotton and corn
- 0.450 kg a.i./ha alfalfa, oats and rye
- 0.565 kg a.i./ha turf grass and canary grass

For private handlers
Cancer risk was less than 1×10^{-6} for all scenarios, except mixing and loading for use on cotton and sorghum (1.3×10^{-6}). It was assumed that all handlers would wear baseline attire and mixers/loaders would wear chemical-resistant gloves in addition to baseline attire.

For commercial handlers
The cancer risk ranged from 1.3×10^{-6} to 1.3×10^{-5} for all scenarios, except application to flax, which was lower (5.4×10^{-7}). It was assumed that all handlers would wear baseline attire and mixers/loaders would wear chemical-resistant gloves in addition to baseline attire.

Aerial

Mixing loading and applying aerially to all crops was assessed at the maximum application rate of 0.565 kg a.i./ha.

Cancer risk for private handlers was as follows:
1.9×10^{-6} for mixers/loaders wearing baseline attire and chemical-resistant gloves
6.2×10^{-7} for applicators wearing baseline attire

Cancer risk for commercial handlers was as follows:
1.9×10^{-5} for mixers/loaders wearing baseline attire and chemical-resistant gloves,
4.8×10^{-6} for applicators wearing baseline attire

Overall, the USEPA concluded that the risk to workers was below the level of concern for all occupational scenarios.

To provide an additional margin of safety, mixers/loaders were required to wear a chemical-resistant apron.

The USEPA required baseline personal protective equipment (PPE) for all uses, in addition to chemical-resistant gloves for cleaning equipment, mixing and loading; additional basic hygiene label statements were recommended.

The RED adequately addressed potential exposure scenarios associated with the Canadian uses of bromoxynil and conclusions derived from the RED are considered applicable to the Canadian situation. Based on this, the PMRA requires baseline protective equipment during handling to further protect workers; additional instructions on good hygiene practices are also required on labels. Proposed label amendments are listed in Appendix III.

3.1.1.2 Postapplication

The postapplication occupational risk assessment considered exposures to workers entering treated sites. Based on the bromoxynil use pattern, it was determined that there was a potential for postapplication exposure to bromoxynil residues for workers. Three scenarios were identified, the first being considered relevant to the Canadian situation:

- workers entering fields following applications to agricultural crops during routine crop procedures (e.g. cultivation, scouting, hoeing);
- workers entering treated commercially grown sod;
- golf course maintenance workers following application to turf grass;
- landscape and ground maintenance workers following applications to commercial/industrial areas and other non-crop areas.

No postapplication exposure data were available to determine potential risks from bromoxynil uses. A surrogate range finder postapplication assessment was performed for occupational settings. The assessment was based on the application rate of 0.565 kg a.i./ha for all crops. Transfer coefficients ranged from low exposure potentials such as hoeing in various field crops (500 cm^2/hr) and scouting early season cotton (1000 cm^2/hr) to high potentials such as harvesting sod (10 000 cm^2/hr). With an acceptable MOE of 100, the restricted entry intervals were 26 days for sod, 4 days for cotton and 0 days for all other crops.

Although based on the risk assessment, the restricted-entry interval (REI) for uses other than cotton and sod was 0 days, the USEPA established a default 24-hour REI for these crops. This was based on the classification of bromoxynil as toxicity category II for eye irritation potential and concerns about risks due to developmental effects and cancer resulting from postapplication activities in crops such as corn and small grains. As most of the applications of bromoxynil made to crops are early in the season, workers entering treated areas after 24 hours for scouting or low-contact labour activities, such as mechanical incorporation and cultivation, should be adequately protected.

This was considered applicable to the Canadian situation and the PMRA requires a 24-hour restricted-entry interval to further protect workers from postapplication exposure. Proposed label amendments are listed in Appendix III.

3.1.2 Aggregate Exposure and Risk Assessment

3.1.2.1 Residential Exposure

Residential uses are not registered in the U.S. or Canada. Thus, no residential exposure is expected from the registered uses of bromoxynil. As such, no residential risk assessment was conducted.

3.1.2.2 Exposure from Food

Acute dietary risk is calculated considering the highest ingestion of bromoxynil that would be likely on any one day and using food consumption and food residue values. A statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of bromoxynil residue that might be consumed in a day. A value representing the high end (99.9^{th} percentile) of this distribution is compared to the acute reference dose (ARfD), which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, then acute dietary exposure is considered to be acceptable.

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada and, in the RED, it was expressed as the chronic population adjusted dose (cPAD). The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation (see Appendix II).

In the case where evidence of carcinogenicity is identified for the active, a cancer potency factor (Q_1^*) is generated and used to estimate cancer risk. The product of the expected exposure and the cancer potency factor (Q_1^*) estimates the lifetime cancer risk as a probability. A lifetime cancer risk that is below 1×10^{-6} usually does not indicate an unacceptable risk for the general population when exposure occurs through pesticide residues in or on food and to otherwise unintentionally exposed persons.

For dietary exposure, the USEPA concluded that the exposure would be to bromoxynil phenol, rather than bromoxynil octanoate or heptanoate, due to conversion of the esters to bromoxynil phenol in the environment. Toxicity endpoints were selected for use in chronic (cancer and non-cancer) and acute (for females 13+ years and all populations except females 13+ years) dietary risk assessments. The endpoints were also appropriate to determine risks from exposure to bromoxynil residues in drinking water.

In the 1998 RED, tolerances were reassessed for several commodities and new tolerances proposed. The USEPA concluded that the qualitative nature of the residue in plants was adequately understood, based on the acceptable alfalfa, sweet corn and transgenic (BXN) cotton metabolism studies conducted using bromoxynil octanoate. The residue of concern in plants other than cotton was defined as bromoxynil per se. The residues of concern in transgenic BXN cotton and cotton commodities (i.e. hulls, meal and cotton gin by-products) were bromoxynil and its metabolite 3,5-dibromo-4-hydroxybenzoic acid (DBHA). The only crop the DBHA metabolite was found in was transgenic cotton. The qualitative nature of the residue in livestock is adequately understood for bromoxynil octanoate based on acceptable ruminant and poultry metabolism studies. The USEPA concluded that the metabolite DBHA could potentially transfer to livestock, as it was found in such feed items. DBHA was assumed to be of equal toxicity and thus residues of concern for livestock were bromoxynil and its metabolite DBHA. The tolerance expression for cotton (and cotton by-products) and livestock took this into account.

Acute dietary risk

An acute (probalistic) dietary analysis was conducted assuming single-day exposure. In the assessment, each person-day of food consumption was matched with randomly selected residue values from field trials submitted in support of the chemical. The assessment assumed that 10% of the cotton crop would be treated and that treated commodities were evenly distributed in the food supply. The assessment used a no observed effect level (NOEL) of 4 mg/kg bw/day, for females 13+ years old and a NOEL of 8mg/kg bw/day, for all populations except females 13+ years old . The calculated MOEs ranged from 24 000 to 82 000, well above the target MOEs of 1000 for females 13+ years old and 100 for all other populations.

The acute risks from dietary exposure were not of concern.

Chronic dietary risk

The USEPA conducted chronic and carcinogenic dietary assessments using cotton residue data submitted by the registrant and anticipated residue levels and percent crop treated for all dietary sources.

A NOEL of 1.5 mg/kg bw was used to assess chronic risk other than cancer. For all population subgroups, less than 1% of the cPAD (0.015 mg/kg bw/day) was consumed. The results of the carcinogenic dietary risk analysis, which incorporated all U.S. uses of bromoxynil, showed a total dietary risk of 1.5×10^{-6}. The USEPA assessment showed that the cotton use added an additional 0.5×10^{-6} risk due to the high residue levels of the metabolite 3,5-dibromo-4-hydroxybenzoic acid (DBHA). DBHA was considered toxicologically equivalent to bromoxynil.

The risks (non-cancer and cancer) from chronic dietary exposure to bromoxynil were not of concern.

This assessment encompassed Canadian uses on wheat, oats, barley, corn, flax, rye, garlic, alfalfa, millet and sorghum and grasses grown for seed, with maximum application rates typically the same or higher in the U.S. compared to Canadian rates. It also included U.S. tolerance levels. A Canadian Maximum Residue Limit (MRL) of 0.1 ppm is established for bromoxynil residues in or on canola, milk, cattle meat and meat by-products, eggs, poultry and poultry by-products. In Canada, residues of bromoxynil on all commodities must not exceed the default, 0.1 ppm.[2] The USEPA assessment is considered conservative for the Canadian situation.

3.1.2.3 Exposure from Drinking Water

Exposure to pesticides through drinking water can occur as a result of groundwater or surface water contamination. Both acute (one-day) and chronic (multiple-year) drinking water risks are considered, using modelling and actual monitoring data, if available, to estimate those risks. Modelling is carried out in tiers of increasing refinement, but is designed to provide high-end estimates of exposure. The risk assessment may be conducted by the "drinking water level of comparison"(DWLOC) approach or a probabilistic assessment in DEEM/Lifeline.

Risk from Drinking Water Exposure

An MOE approach, not unlike that used for the occupational risk, was used to estimate the acute risk from exposure to bromoxynil in drinking water. Chronic risk from drinking water was estimated by determining how much of a pesticide residue in water may be ingested daily and this potential exposure was compared to an ADI, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects.

Groundwater

The USEPA concluded that the potential for groundwater contamination (and exposure) from bromoxynil was extremely low (see Section 3.2.1)

Surface water

To estimate dietary exposure from surface waters, the USEPA examined water monitoring data from the United States Geological Survey (USGS) NAWQA Program, reported between 1993 and 1995 from 7 of 20 river basins (primarily agricultural use) throughout the U.S. The maximum concentration of bromoxynil in surface water was 6.1 ppb (12.2 ppb, when accounting for 50% recovery, was used in the acute assessment). Bromoxynil was not detected in surface waters for urban land use.

---

2 Changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be promulgated.

For the purpose of estimating a reasonable high-end exposure for the chronic drinking water assessment, the USEPA focussed on the calculated time-weighted annual mean concentration at 11 USGS monitored sites. The sites chosen were located in watersheds likely to have bromoxynil use. These time-weighted annual mean concentrations (not corrected for the analytical recovery rate of 50%) ranged from 0.011 ppb to 0.18 ppb with 10 of the 11 sites having concentrations below 0.05 ppb. Six of the ten sites had time-weighted annual mean concentrations at or below 0.014 ppb. Therefore, to estimate chronic exposure from surface sources of drinking water, the USEPA used 0.05 ppb, which is considered a high-end estimate.

Consumption of two litres per day of water was assumed for an adult male (70 kg) and female (60 kg), while children (10 kg) were assumed to drink one litre.

The drinking water risks from acute and chronic (cancer and non-cancer) exposure for the population subgroups were determined. Acute MOEs for all groups were greater than 10 000 (target was 1000 for females 13+ and 100 for all other populations). Chronic non-cancer risk was less than 1% of the RfD. The cancer risk from drinking water was 0.2×10^{-6} for adult males and females.

Environmental concentrations (EECs) were also modelled using the Pesticide Root Zone Model version 2.3 and Exposure Analysis Modeling System Version 2.94 (PRZM-EXAMS) based on cotton use, as this was the most conservative scenario for surface water exposure. Based on model estimates, the maximum or peak estimated concentration for bromoxynil was 12.3 ppb and the maximum estimated long-term mean was 0.24 ppb (using 36 years of weather data). The reported values were what might be expected in a small water body near a cotton field highly prone to runoff. The modelling data's peak estimate, corroborated the estimated peak concentration in the monitoring program.

The USEPA concluded that there are no chronic or acute risks of concern for any subpopulations from drinking water.

The modelled results were based on the worst case scenario of cotton use. Use of bromoxynil on tolerant cotton in the U.S. represents the most conservative scenario for drinking water exposure and this conservatively encompasses the Canadian drinking water exposure situation.
The PMRA reviewed existing water monitoring data. Available water monitoring concentrations were below the Canadian water quality guidelines for the protection of aquatic life (CCME (2002)) and the interim drinking water quality (Health Canada (1989)) guidelines of 5000 ng/L. Based on this, USEPA EECs are considered to encompass the Canadian situation.

3.1.2.4 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to bromoxynil (i.e. from food, water and residential exposures). Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures. Short- and intermediate-term aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

The aggregate risk estimate was based on exposure from food and water only, for the most highly exposed population subgroups (females 13+ and children 1–6 years) and the general population as appropriate (no residential uses registered in the U.S.). Calculated MOEs for acute aggregate exposure to the population subgroups ranged from > 5000 to > 16 000. The chronic non-cancer aggregate risks were estimated to be less than 1% of the cPAD for all groups; the cancer aggregate risks were estimated to be 1.7×10^{-6} for the whole American population. The USEPA concluded that these estimated risks were below the level of concern and that the aggregate cancer risk from bromoxynil was acceptable.

Canadian use sites, application rates and forms of bromoxynil are encompassed by the U.S. use patterns eligible for reregistration. The U.S. dietary risk assessments used field trial residues as a result of the application of the maximum seasonal rate for crops. In Canada, the registered maximum rate for all crops is lower than in the U.S.

Overall, the Canadian potential aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of bromoxynil in Canada.

There was sufficient information to make a determination of eligibility for reregistration of U.S. products with both esters of bromoxynil. Both esters were deemed to be toxicologically equivalent and are expected to convert readily to the phenol, and the USEPA's dietary risk determination was based on bromoxynil phenol. The inference can be made here that conclusions on risk from dietary exposure relevant to the octanoate ester (and ester mixture) would be relevant to Canadian products with only bromoxynil heptanoate.

Canadian end-use products containing bromoxynil registered for food/feed use must, according to REG2001-05 (PMRA 2001), indicate the following:

- "If this pest control product is to be used on a commodity that may be exported to the U.S., and you require information on acceptable residue levels in the U.S., contact 1-866-375-4648 or www.croplife.ca/."

3.1.3 Cumulative Effects

The USEPA has not determined whether bromoxynil has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that bromoxynil does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required. These conclusions are considered applicable to the Canadian situation.

3.2 Environment

3.2.1 Environmental Risk Assessment

The USEPA found bromoxynil octanoate to be chemically and physically similar to bromoxynil heptanoate. The conclusions on environmental fate of bromoxynil octanoate were relevant to the heptanoate form. Although bromoxynil is mobile, it is not expected to persist in the environment as both esters readily hydrolyse to bromoxynil phenol. Based on the rapid aerobic and anaerobic conversion of bromoxynil phenol to CO_2, it too would have low potential for groundwater contamination. Thus, based on environmental fate studies, the USEPA concluded bromoxynil octanoate or heptanoate should not persist in surface waters nor should it be a concern for groundwater contamination.

To assess the ecological risk of bromoxynil to both terrestrial and aquatic non-target plants and animals, the USEPA calculated risk quotients (RQs) based on appropriate toxicity endpoints and expected environmental concentrations (EECs), and compared the resulting RQs to acute and chronic levels of concern (LOCs).

For its assessments, the USEPA used toxicity data for bromoxynil octanoate (with the exception of aquatic vascular plants where the heptanoate ester was used) to estimate risk. Bridging data for bromoxynil octanoate were used to make a determination of risks from the use of the heptanoate ester.

Bromoxynil residue levels on dietary items for birds (i.e. grasses, broadleaf plants, insects, fruits and pods) following single typical (0.448 kg a.i./ha) and multiple maximum (3×0.565 kg a.i./ha) application rates were estimated to predict hazard to birds. Estimates were based on the work of Hoerger and Kenaga (1972) as modified by Fletcher et al. (1994) and an acute LC_{50} of 1150 ppm and a NOEL of 102 ppm. It was assumed mammals would be exposed to dietary residues similar to birds and EECs calculated for birds were used to estimate exposure to mammals. Risks were determined for meadow voles consuming short grasses, adult field mice consuming seeds and the least shrew consuming insects, using an LD_{50} of 238 mg/kg and a NOEL of 50 ppm.

Aquatic EECs were calculated using the Generic Estimated Environmental Concentration Program (GENEEC) for bromoxynil octanoate application (by groundboom and aerially) to corn, small grains and cotton. Both typical and maximum rates were used and they ranged from a typical single application for corn at 0.313 kg a.i./ha to a maximum of three applications at 0.565 kg a.i./ha for cotton use. Appropriate endpoints were selected for marine or freshwater fish and invertebrates from toxicity studies. In addition, to further address the risk to aquatic organisms from bromoxynil octanoate application to transgenic cotton, the USEPA used Tier 2 PRZM-EXAM modelling to estimate EECs.

Terrestrial vertebrates (birds and mammals)
The avian acute LOC for endangered species (0.1) was exceeded for all use rates on short grasses (from 0.3 at maximum rate multiple applications to 0.4 at a single application) and on broadleaf plants and insects (0.12 for maximum rate multiple applications). The risks quotient for the maximum rate (with multiple applications) on short grasses exceeded the restricted chronic LOC (0.2) by a small margin. Endangered birds may be affected acutely by use of bromoxynil octanoate, but overall it was expected to pose minimal risk to avian species.

The USEPA concluded that bromoxynil octanoate could potentially impair the reproduction of birds at dietary concentrations greater than 102 ppm. For both single and multiple applications, the chronic LOC (1) for endangered and non-endangered species was exceeded for the two highest use rates on short grasses and broadleaf plants and insects. The USEPA determined that the use of bromoxynil octanoate may have a chronic effect on endangered birds. At the time of the RED, no chronic avian data for bromoxynil phenol were available. However, the phenol was substantially less acutely toxic than the octanoate and the assumption was made that the phenol would also be less toxic on a chronic basis than the octanoate ester. It was concluded that the chronic risk to birds from bromoxynil phenol, heptanoate or octanoate would likely be low.

Some LOCs of risk to endangered species were exceeded for the higher application rates for the vole, field mouse and least shrew. However, the acute risk to mammals, including threatened and endangered species, from exposure to bromoxynil octanoate was expected to be low.

All of the chronic RQs on all food items, except fruits and pods, exceeded the LOC for all use rates. The USEPA concluded that chronic risk to mammals, including endangered species, would be expected to be high if mammals were exposed to high enough residues of bromoxynil octanoate. However, such levels are unlikely to occur from the registered uses.

Terrestrial insects
Bromoxynil octanoate was found to be practically non-toxic to honeybees on an acute basis; therefore, minimal risk was presumed.

Terrestrial plants
Tier II plant toxicity data for bromoxynil octanoate and heptanoate indicates that non-target terrestrial plants may be affected from runoff if the soil residues exceed an equivalent of 0.13 kg a.i./ha, and from drift if the drift residues exceed 0.019 kg a.i./ha. The USEPA expected the overall risk to both endangered and non-endangered terrestrial plants to be medium. The LOCs were exceeded for spray drift from aerial application of bromoxynil octanoate at the maximum label rate. The USEPA stated that although the LOCs were only exceeded by a small margin, the risk to these plants is likely underestimated because the model did not take into account multiple applications.

Aquatic plants
The USEPA reviewed Tier II nonvascular plant toxicity data for bromoxynil octanoate and heptanoate and concluded that algae and diatoms were sensitive to both bromoxynil forms. Risk to aquatic vascular plants from the use of bromoxynil octanoate was uncertain at the time of the RED. However, the USEPA assessed the risk to these plants (based on data from bromoxynil heptanoate) and concluded they are not likely to be affected by the use of either ester.

The LOC for endangered plant species was met but not exceeded from cotton use. The risk to these plants was expected to be medium. Overall, the USEPA concluded that risk to aquatic plants from the worst case scenario (cotton use) was expected to be low.

Fish (freshwater and estuarine/marine)
The USEPA determined that LOCs would only be slightly exceeded for endangered fish species based on results from all modelled use sites, but were likely to be at risk only during the short time before the esters (octanoate and heptanoate) degrade to phenol and ultimately to CO_2. Thus, the overall acute risks to freshwater and estuarine fish were expected to be low.

No chronic data for estuarine species were submitted. Data from the freshwater studies were used to determine risk because, in acute studies, freshwater species were shown to be more sensitive. No LOCs were exceeded for freshwater and estuarine fish from any uses of bromoxynil octanoate. The USEPA concluded, however, that as bromoxynil octanoate readily degrades to the phenol, which further degrades to CO_2, bromoxynil octanoate was not expected to remain in water long enough to cause chronic adverse effects. Overall, the chronic risk to endangered and non-endangered freshwater and estuarine species was likely to be minimal. PRZM-EXAM modelling data corroborated the minimal risk expected to fish from even the most conservative scenario, cotton use, as no LOCs were exceeded.

Aquatic invertebrates (freshwater and estuarine/marine)
Based on the aquatic invertebrate maximum allowable toxic concentration (MATC) from the Daphnia life cycle study (3.7 ppb) and 21-day GENEEC EECs, the USEPA concluded that the use of bromoxynil octanoate represented minimal chronic risk to freshwater invertebrates.

The cotton use exceeded the acute high risk LOC to freshwater invertebrates. The USEPA concluded that overall acute risk to aquatic invertebrates was expected to be medium.

The acute LOC for endangered shrimp species was exceeded only by a small margin for bromoxynil octanoate when applied to cotton (both typical and maximum rates). Therefore, endangered estuarine shrimp species may be affected. The USEPA expected the overall acute risk to estuarine invertebrates to be low.

No chronic LOCs were exceeded for any uses for freshwater invertebrates. No chronic estuarine data were available. However, because the USEPA determined freshwater species to be more sensitive to bromoxynil, freshwater invertebrate data were used to draw conclusions concerning chronic effects to estuarine species.

Overall, the USEPA concluded chronic risk to freshwater and estuarine invertebrates was expected to be minimal.

The USEPA required no risk mitigation as a result of environmental risk assessments. It was stated that though levels of concern (LOCs) were slightly exceeded, generally the risks to the environment from the use of bromoxynil octanoate and heptanoate were relatively low.

The U.S. use pattern for bromoxynil encompasses the Canadian use pattern, and any risk-reduction measures recommended by the USEPA should be applied to Canadian bromoxynil products. The risk determined from the use of the octanoate ester and heptanoate ester are also considered relevant to Canadian products with heptanoate only.

- The PMRA will require terrestrial and aquatic buffer zones for the emulsifiable concentrate or emulsion formulations of bromoxynil to protect aquatic organisms and terrestrial plants from spray drift. Inputs to buffer zone models are described in Appendix IV.

Proposed label amendments are listed in Appendix III.

3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's Toxic Substances Management Policy (TSMP), which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

The federal Toxic Substances Management Policy and the Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of bromoxynil with the following conclusions:

- Bromoxynil phenol does not meet the TSMP Track 1 cut-off criterion for bioaccumulation with an *n*-octanol–water partition coefficient (log K_{ow}) of 2.8. Therefore, bromoxynil is not considered to be a candidate for Track 1 classification. Although the log K_{ow} for the octanoate and heptanoate form is > 5, bioconcentration factors (bromoxynil octanoate) of 63× for edible tissue, 400× for inedible tissue and 230× for whole fish were reported by the USEPA. Thus, neither bromoxynil octanoate nor heptanoate would be candidates for Track 1 classification.

- Based on a review of the available chemistry information (see Section 2.1), the technical product is not expected to contain impurities of toxicological concern, as identified in Regulatory Directive DIR98-04, or TSMP Track 1 substances, as identified in Regulatory Directive DIR99-03, Appendix II.

- Formulant issues are being addressed through the PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document*, published on 31 May 2006.

- No other impurities of toxicological concern, as identified in Section 2.13.4 of Regulatory Directive DIR98-04, or TSMP Track 1 substances, as identified in Appendix II of Regulatory Directive DIR99-03, are expected to be present in the technical product of bromoxynil.

4.0 OECD Status of Bromoxonil

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which includes 30 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policy. They compare experiences, share information and analyses, seek answers to common problems and work to coordinate domestic and international policies to allow for consistency in practices across nations.

Based on the currently available information on the status of bromoxynil in other OECD member countries, it was reviewed by the European Commission and approved for inclusion in the list of active ingredients authorized for use as plant protection products in the European Union (EC, 2004c).

It has been prohibited from use as a pesticide in Norway based on unacceptable risk to the applicator, its toxicity to aquatic organisms and because there were "already alternatives on the market that pose a lower risk to human health" (PIC circular XIV, 2001).[3] In Sweden, bromoxynil was withdrawn from the market in 1994 due to "teratogenic effects in experimental animals" (KEMI, 1998).

---

[3] PIC circulars are published by the Rotterdam Convention Secretariat; under this Convention, parties to the Convention have committed to inform other parties about legislative bans or severe restrictions on the use of chemicals and to notify recipient countries of any exports of regulated substances. This procedure is called Prior Informed Consent (PIC). When a party has adopted a final regulatory action to ban or severely restrict a chemical, the party notifies the Rotterdam Convention Secretariat; notifications are published in PIC circulars.

As described earlier in this document, the United States, also an OECD member, conducted an assessment of the registration of all bromoxynil uses in 1998 and concluded that uses of bromoxynil as a pesticide do not result in unreasonable adverse effects to human health or the environment provided the risk-reduction measures recommended in the Reregistration Eligibility Decision (RED) document are implemented. The evaluation included occupational and environmental risk assessments. The USEPA considered the human carcinogenic potential of bromoxynil, and to lower the risk to human health, required additional personal protective equipment for pesticide handlers. In addition, re-entry to treated areas was restricted and monitoring data were also required to ensure that if bromoxynil is present in drinking water sources, it is at acceptable levels.

The USEPA considered bromoxynil toxic to aquatic organisms, highly mobile but not persistent in the environment. It concluded that after application, both bromoxynil esters rapidly break down to the less toxic phenol, which subsequently breaks down to carbon dioxide. The USEPA required no risk mitigation as a result of environmental risk assessments.

As also indicated in this document, the Canadian re-evaluation of bromoxynil is largely based on the 1998 USEPA assessments. As described in Section 3.2.1 above, the PMRA has found the USEPA human health and environmental risk conclusions to be relevant to the Canadian uses of bromoxynil and requires measures to mitigate human health risks, as well as additional environmental hazard label statements and aquatic and terrestrial buffer zones of 1 to 55 metres.

A search of bromoxynil water monitoring data in Canada revealed that this pesticide has been analyzed and detected in surface water in the provinces of Alberta, Manitoba, Saskatchewan, Ontario and Quebec. No data were available from groundwater sources.

The available monitoring data fail to meet the Canadian water quality guidelines for the protection of aquatic life (CCME (2002)) and the interim drinking water quality (Health Canada (1989)) guidelines of 5000 ng/L.

Therefore, concerns identified in the OECD (i.e. Sweden and Norway) relating to human health or environmental properties of the active ingredient bromoxynil were taken into consideration in the Canadian re-evaluation and have been addressed in the proposed Canadian re-evaluation decision.

5.0 Proposed Regulatory Decision

The PMRA has determined that bromoxynil is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. Canadian end-use product labels should be amended to include label statements listed in Appendix III. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision.

Bromoxynil end-use products that contain more than one active ingredient under re-evaluation will be eligible for reregistration only when all of those other active ingredients are also determined to be eligible for reregistration.

6.0 Data Required as Condition of Continued Registration

No data are required as a condition of continued registration.

7.0 Supporting Documentation

PMRA documents, such as DIR2001-03 and DACO tables, can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1 613-736-3799 outside Canada (long distance charges apply); Fax: 613-736-3798; E-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document bromoxynil, (EPA-738-R-98-013) is available on the Office of Pesticide Programs website at www.epa.gov/pesticides/reregistration under Chemical Status.

List of Abbreviations

°C	degree(s) Celsius
ADI	acceptable daily intake
a.i.	active ingredient
ARfD	acute reference dose
ARI	aggregate risk index
ARTF	Agricultural Re-entry Task Force
atm	atmosphere(s)
bw	body weight
CAS	Chemical Abstracts Service
CFIA	Canadian Food Inspection Agency
cPAD	chronic population adjusted dose (cPAD)
cm	centimetre(s)
d	day(s)
DACO	data code
DEEM™	Dietary Exposure Evaluation Model
DER	Data Evaluation Report
DFR	dislodgeable foliar residue
DT_{50}	dissipation time to 50%
DWLOC	drinking water level of comparison
EEC	estimated environmental concentration
EXAMS	Exposure Analysis Modeling System
F_0	parental generation
F_1	first filial generation
F_2	second filial generation
FQPA	*Food Quality Protection Act*
g	gram(s)
GENEEC	Generic Estimated Environmental Concentration
h	hour(s)
ha	hectare
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LEACHM	Leaching Estimation and Chemistry Model
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
LOEC	lowest observed effect concentration
LOEL	lowest observed effect level
m	metre(s)
m^3	metre(s) cubed
MATC	maximum allowable toxic concentration
min	minute(s)

mg	milligram(s)
mm	millimetre(s)
mm Hg	millimetre mercury
MOE	margin of exposure
MRL	maximum residue limit
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
nm	nanometre
OC	organic carbon
OECD	Organisation for Economic Co-operation and Development
OP	organophosphate
PACR	Proposed Acceptability for Continuing Registration
PCP	pest control product
PDI	potential daily intake
PHI	preharvest interval
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PIC	Prior Informed Consent
pKa	-log10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
PRZM	Pesticide Root Zone Model
Q*	cancer potency factor
RED	Reregistration Eligibility Decision
REI	restricted-entry interval
RfD	reference dose
RQ	risk quotient
SP	soluble powder
TC	transfer coefficient
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
URMULE	User Requested Minor Use Label Expansion
U.S.	United States
USEPA	United States Environmental Protection Agency
USDA	United States Department of Agriculture
USFDA	United States Food and Drug Administration
USGS	United States Geological Survey

Appendix I Registered Bromoxynil Products as of 31 July 2007

Registration Number	Class	Registrant Name	Product Name	Bromoxynil Form Present	Formulation Type	Guarantee g/L
9510	Commercial	Bayer Cropscience Inc.	BUCTRIL M emulsifiable selective weedkiller	Octanoate	Emulsifiable Concentrate or Emulsion	200 200
14878	Commercial	Bayer Cropscience Inc.	PARDNER emulsifiable selective weedkiller	Heptanoate	Emulsifiable Concentrate or Emulsion	225
16164	Commercial	Makhteshimagan of North America	BADGE emulsifiable selective weedkiller	Octanoate	Emulsifiable Concentrate or Emulsion	225 225
17145	Commercial	Bayer Cropscience Inc.	BROMOX 450M EMULSIFIABLE HERBICIDE	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	225 225
17507	Commercial	Bayer Cropscience Inc.	HOE-GRASS II EMULSIFIABLE LIQUID HERBICIDE	Octanoate	Emulsifiable Concentrate or Emulsion	80 230
18001	Commercial	Bayer Cropscience Inc.	PARDNER emulsifiable selective weedkiller	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	280
18022	Commercial	Bayer Cropscience Inc.	BUCTRIL M emulsifiable selective weedkiller	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	280 280
22659	Commercial	Bayer Cropscience Inc.	THUMPER emulsifiable selective weedkiller	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	280 280
24497	Commercial	Bayer Cropscience Inc.	UNITY 280 EC emulsifiable selective weedkiller	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	280
24870	Commercial	Bayer Cropscience Inc.	BROMINAL M emulsifiable selective weedkiller	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	280 280
24877	Commercial	Bayer Cropscience Inc.	BROMOX 560M emulsifiable selective weedkiller	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	280 280
25311	Commercial	Bayer Cropscience Inc.	IPCO BUCTRIL M emulsifiable selective weedkiller	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	280 280
25341	Commercial	Nufarm Agriculture Inc.	Nufarm Karil 235 liquid herbicide	Octanoate	Emulsifiable Concentrate or Emulsion	235
25342	Commercial	Nufarm Agriculture Inc.	Nufarm Mextrol 400M herbicide	Octanoate	Emulsifiable Concentrate or Emulsion	200 200

Registration Number	Class	Registrant Name	Product Name	Bromoxynil Form Present	Formulation Type	Guarantee g/L
25791	Commercial	Bayer Cropscience Inc.	Compas 480 emulsifiable selective weedkiller	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	480
26184	Commercial	Bayer Cropscience Inc.	Platinum 560EC broadleaf herbicide	Octanoate and heptanoate	Emulsifiable Concentrate or Emulsion	280 280
26999	Commercial	Nufarm Agriculture Inc.	Mextrol 450M liquid herbicide	Octanoate	Emulsifiable Concentrate or Emulsion	225 225
28109	Commercial	Interprovincial Coop Ltd.	IPCO logic M liquid herbicide	Octanoate	Emulsifiable Concentrate or Emulsion	225 225
28123	Commercial	Nufarm Agriculture Inc.	Approve Herbicide	Octanoate	Emulsifiable Concentrate or Emulsion	225 225
28276	Commercial	Makhteshimagan of North America	Bromotril 240 EC emulsifiable selective weedkiller	Octanoate	Emulsifiable Concentrate or Emulsion	240
24403	Manufacturing Concentrate	Bayer Cropscience Inc.	BROMOXYNIL MIXED ESTER SOLUTION 50% (MEO 50%) manufacturing concentrate	Octanoate and heptanoate	Solution	50%
24404	Manufacturing Concentrate	Bayer Cropscience Inc.	BROMOXYNIL MIXED ESTER SOLUTION 60% (MEO 60%) manufacturing concentrate	Octanoate and heptanoate	Solution	60%
24471	Manufacturing Concentrate	Bayer Cropscience Inc.	BROMOXYNIL MIXED ESTER SOLID manufacturing concentrate	Octanoate and heptanoate	Solid	66.3%
19693	Technical	Bayer Cropscience Inc.	BROMOXYNIL TECHNICAL	Phenol	Solid	97.5%
19700	Technical	Bayer Cropscience Inc.	BROMOXYNIL HEPTANOATE TECHNICAL	Heptanoate	Not Applicable or Not Available	68.2%
19705	Technical	Bayer Cropscience Inc.	BROMOXYNIL OCTANOATE TECHNICAL	Octanoate	Solid	64.6%

Registration Number	Class	Registrant Name	Product Name	Bromoxynil Form Present	Formulation Type	Guarantee g/L
19975	Technical	Bayer Cropscience Inc.	BROMOXYNIL TECHNICAL (FOR MANUFACTURING PURPOSES)	Phenol	Solid	98.5%
19978	Technical	Bayer Cropscience Inc.	TECHNICAL BROMOXYNIL OCTANOATE	Octanoate	Solid	66.3%
21926	Technical	Nufarm Agri. Inc.	Nufarm BROMOXYNIL PHENOL	Phenol	NA	98%
21927	Technical	Nufarm Agriculture Inc.	Nufarm bromoxynil octanoate technical	Octanoate	Emulsifiable Concentrate or Emulsion	65.5%
27675	Technical	Makhteshimagan of North America	Bromotril technical (octanoate)	Octanoate	Solid	66.1%

Appendix II Summary of Toxicological Endpoints Selected by the USEPA for Bromoxynil Health Risk Assessment

Exposure Duration	Exposure Route	Endpoint
Acute females 13+	Dietary	Developmental NOEL of 4 mg/kg/day (rat oral) (phenol) MOE = 1000
Acute general population (except females 13+)	Dietary	Systemic NOEL of 8 mg/kg/day (dog oral) (phenol) MOE = 100
Chronic (non-cancer)	Dietary	NOEL/LOEL 1.5 mg/kg/day (dog oral) (phenol) UF = 100 cPAD = 0.015 mg/kg/day
Chronic (cancer)	Dietary	Q_1* = 0.103 (mg/kg/day) (mice oral) (phenol)
Short-term occupational	Dermal	Developmental NOEL of 10 mg/kg/day (rat dermal) (octanoate) MOE = 100
Intermediate-term occupational	Dermal	Developmental NOEL of 10 mg/kg/day (rat dermal) (octanoate) MOE = 100
Chronic occupational (non-cancer)	Dermal	Developmental NOEL of 10 mg/kg/day (rat dermal) (octanoate) MOE = 100
Carcinogenic potential occupational	Dermal	Q_1* = 0.103 (mg/kg/day) (mice oral) (phenol)

Appendix III Label Amendments for Products Containing Bromoxynil

The **GENERAL USE PRECAUTIONS** section of all end-use products must include the following statement:

- "If this pest control product is to be used on a commodity that may be exported to the U.S. and you require information on acceptable residue levels in the U.S., contact 1-866-375-4648 or www.cropro.org/."

Canadian end-use product labels should be amended to include the following statements to further protect workers and the environment.

Add to the USE PRECAUTIONS section of all end-use products the following statements:

- "All handlers must wear a long-sleeved shirt and long pants. In addition, wear chemical-resistant gloves and a chemical-resistant apron during mixing/loading activities. Chemical-resistant gloves should also be worn during repair and clean-up activities."

- "Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 24 hours."

- "Do not apply this product in a way that this product will contact workers or other persons, either directly or through drift. Only handlers wearing personal protective equipment may be in the area being treated during application."

- "Discard clothing or other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them."

- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."

Add to ENVIRONMENTAL HAZARDS:

TOXIC to aquatic organisms and non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE.

Add to DIRECTIONS FOR USE:

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground.

Aerial application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 16 km/h at flying height at the site of application. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length **MUST NOT** exceed 65% of the wingspan or rotorspan.

Buffer zones:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer, inter-row hooded sprayer, spot treatment, soil drench and soil incorporation.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands), sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of Application	Crop		Buffer Zones (metres) Required for the Protection of:				
			Freshwater Habitat of Depths:		Estuarine/Marine Habitats of Depths:		Terrestrial Habitat
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m	
Field sprayer*	All crops		1	1	1	1	1
Aerial	Oats	Fixed wing	15	2	1	1	50
		Rotary wing	15	1	1	1	45
	Barley and wheat	Fixed wing	20	5	1	1	55
		Rotary wing	20	3	1	1	45

* For field sprayer application, buffer zones can be reduced with the use of drift-reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy, the labelled buffer zone can be reduced by 30%.

When a tank mixture is used, consult the labels of the other tank-mix ingredients and observe the largest (most restrictive) buffer zone of the products included in the tank mixture.

The label amendments above do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

Appendix IV Inputs to Buffer Zone Models

Ground Use Data (from Canadian labels)				
Crop	Formulation Type	Method of Application	Number of Applications	Maximum Application Rate (g a.i./ha)
Alfalfa, corn, oats	Emulsion	Field sprayer	2	337.5
Barley , wheat	Emulsion	Field sprayer	2	281
Garlic, flax	Emulsion	Field sprayer	1	280
Rye, triticale	Emulsion	Field sprayer	1	338
Seedling grasses	Emulsion	Field sprayer	1	336
Grasses grown for forage	Emulsion	Field sprayer	1	280
Oats	Emulsion	Aerial	1	281
Barley	Emulsion	Aerial	1	338
Zero till barley	Emulsion	Aerial	2	338

Model Input Data for Aquatic Buffer Zones (from 1998 RED)		
Half life for aquatic buffer zones	1 day	
Most sensitive freshwater species	*Bluegill sunfish*	1/10 LC_{50}= 0.0029mg/L
Most sensitive estuarine/marine species	*Sheepshead minnow*	1/10 LC_{50} = 0.017 mg/L
End point for amphibians	*Fathead minnow*	NOEC = 0.009 mg/L

Model Input Data for Terrestrial Buffer Zones (from 1998 RED)		
Half life for terrestrial buffer zones	Soil degradation half-life	2 days
Most sensitive terrestrial plant species EC_{25} for vegetative vigour	Cabbage – Vegetative vigour	12.3 g ai/ha